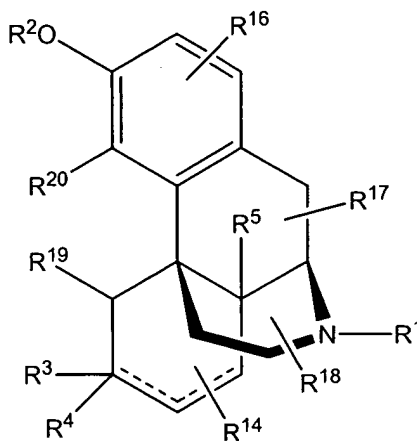


Claims:

1. A pharmaceutically acceptable salt of a codrug, wherein the codrug comprises:
 - a) a first drug moiety having a first biological activity, or a prodrug form thereof, including a basic nitrogen,
 - b) a second drug moiety having a second biological activity, or a prodrug form thereof, and
 - c) a linkage covalently linking said first and second drug moieties to form said codrug, said linkage being cleaved under physiological conditions to regenerate said first and second drug moieties as active agents having said first and second biological activities,wherein the salt of the codrug has a decomposition rate at room temperature at least 50% lower than the decomposition rate of said codrug as a free base.
2. The salt of a codrug according to claim 1, wherein the first drug moiety is an opioid.
3. The salt of a codrug according to claim 1 or 2, wherein the second drug moiety is an antidepressant compound, an analgesic compound, a steroid, a non-steroidal antiinflammatory drug (NSAIDs), an antibiotic compound, an anti-fungal compound, an antiviral compound, an antiproliferative compound, an antiglaucoma compound, an immunomodulatory compound, a cell transport/mobility impeding agent, a cytokine, a peptide, a protein, an antimetabolite compound, an antipsoriatic compound, a keratolytic compound, an anxiolytic compound, an antipsychotic compound, an alpha-blocker compound, an anti-androgen compound, an anticholinergic compound, an adrenergic compound, a purinergic compound, a dopaminergic compound, a vanilloid compound, or an anti-cancer compound.
4. The salt of a codrug according to claim 2, wherein the opioid is morphine or a morphine derivative.

5. The salt of a codrug according to claim 4, wherein the active form of the opioid is represented in the general formula (I):



(I)

5 wherein

R¹ represents a hydrogen, a C₁₋₆-alkyl group, a C₃₋₆-cycloalkyl-C₁₋₆-alkyl group, a C₁₋₆-alkenyl group, a C₁₋₆-alkanoyl group, a C₃₋₆-cycloalkenyl-C₁₋₆-alkyl group, a C₃₋₆-cycloalkyl-C₁₋₆-alkanoyl group, a C₃₋₆-cycloalkenyl-C₁₋₆-alkanoyl group, an Ar-C₁₋₆-alkyl group, or an allyl group;

10 R² represents H, a C₁₋₆-alkyl group, or a C₁₋₆-alkanoyl group;

R³ represents a hydrogen, a C₁₋₆-alkylthio group, an aryl group, a C₁₋₆-alkoxycarbonylalkyl group, a C₁₋₆-alkyl group, a hydroxyl group, an azido group, a C₁₋₁₂-alkanoyl group, an amine NR^d₂ wherein R^d is hydrogen or Ar, or C(=O)NH₂ when R⁴ is a hydrogen, or an oxo group or =NOH when R⁴ is absent;

15

R⁴ is absent or represents a hydrogen;

R⁵ represents a hydrogen, a hydroxyl group, a lower alkyl group, an amine NR_aR_b wherein R_a is a hydrogen, alkyl C₁₋₁₂, alkenyl C₃₋₈, cycloalkyl C₃₋₇ alkyl C₁₋₄, Ar-alkyl C₁₋₅ or Ar-alkenyl C₃₋₅, provided that R_a does not contain the system -CH=CH- attached to the nitrogen atom; and R_b is hydrogen, alkyl C₁₋₈, or the group COR_c wherein R_c is a hydrogen, alkyl C₁₋₁₁, alkenyl C₂₋₇, Ar, Ar-alkyl C₁₋₅, Ar-alkenyl C₂₋₅, cycloalkyl C₃₋₈, or cycloalkyl C₃₋₈ alkyl C₁₋₃;

20

or R⁴ and R⁵ taken together represent -(CH₂)₂-;

R¹⁴ represents a hydrogen, a lower alkyl group, a halogen group, or -C(-OH)(-R¹⁵)₂;

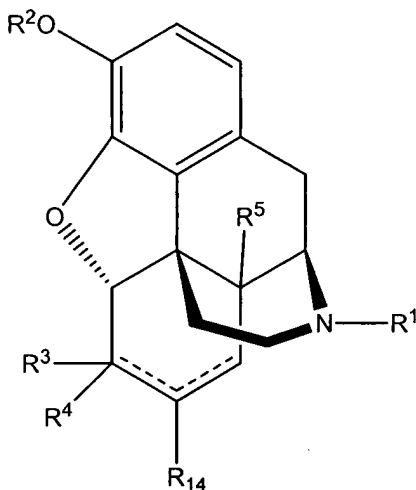
R^{15} independently for each occurrence represents a lower alkyl;

R^{16} , R^{17} , and R^{18} each independently represent a hydrogen, a lower alkyl group, or a halogen group;

R^{19} and R^{20} each represent hydrogen or together represent the oxygen of a
5 dihydrofuran ring;

Ar is phenyl or phenyl substituted by halogen, alkyl C_{1-3} , hydroxyl or alkoxy C_{1-3} ;
and the dotted line indicates an optional bond.

6. The salt of a codrug according to claim 4, wherein the active form of the opioid is represented in the general formula (II):



10

(II)

wherein

R^1 represents a hydrogen, a C_{1-6} -alkyl group, a C_{3-6} -cycloalkyl- C_{1-6} -alkyl group, a
 C_{1-6} -alkenyl group, a C_{1-6} -alkanoyl group, a C_{3-6} -cycloalkenyl- C_{1-6} -alkyl
15 group, a C_{3-6} -cycloalkyl- C_{1-6} -alkanoyl group, a C_{3-6} -cycloalkenyl- C_{1-6} -
alkanoyl group, an Ar- C_{1-6} -alkyl group, or an allyl group;

R^2 represents a hydrogen, a C_{1-6} -alkyl group, or a C_{1-6} -alkanoyl group;

R^3 represents a hydrogen, a C_{1-6} -alkylthio group, an aryl group, a C_{1-6} -
alkoxycarbonylalkyl group, a C_{1-6} -alkyl group, a hydroxyl group, an azido
20 group, a C_{1-12} -alkanoyl group, an amine NR^d_2 wherein R^d is hydrogen or Ar,
or $C(=O)NH_2$ when R^4 is a hydrogen, or an oxo group or $=NOH$ when R^4 is
absent;

- R^4 is absent or represents a hydrogen;
- R^5 represents a hydrogen, a hydroxyl group, a lower alkyl group, an amine NR_aR_b wherein R_a is a hydrogen, alkyl C_{1-12} , alkenyl C_{3-8} , cycloalkyl C_{3-7} alkyl C_{1-4} , Ar-alkyl C_{1-5} or Ar-alkenyl C_{3-5} , provided that R_a does not contain the system
- 5 $-CH=CH-$ attached to the nitrogen atom; and R_b is hydrogen, alkyl C_{1-8} , or the group COR_c wherein R_c is a hydrogen, alkyl C_{1-11} , alkenyl C_{2-7} , Ar, Ar-alkyl C_{1-5} , Ar-alkenyl C_{2-5} , cycloalkyl C_{3-8} , or cycloalkyl C_{3-8} alkyl C_{1-3} ;
- or R^4 and R^5 taken together represent $-(CH_2)_2-$;
- R^{14} represents a hydrogen, a lower alkyl group, a halogen group, or $-C(-OH)(-R^{15})_2$;
- 10 R^{15} independently for each occurrence represents a lower alkyl;
- Ar is phenyl or phenyl substituted by halogen, alkyl C_{1-3} , hydroxyl or alkoxy C_{1-3} ; and the dotted line indicates an optional bond.

7. The salt of a codrug according to claim 4, wherein the active form of the opioid is selected from apomorphine, buprenorphine, codeine, dihydrocodeine,

15 dihydroetorphine, diprenorphine, etorphine, hydrocodone, hydromorphone, levorphanol, meperidine, metopon, o-methylnaltrexone, morphine, naloxone, naltrexone, normorphine, oxycodone, and oxymorphone.

8. The salt of a codrug according to claim 2, wherein the opioid is fentanyl or a fentanyl derivative.

20 9. The salt of a codrug according to claim 2, wherein the opioid is selected from alfentanil, β -hydroxy-3-methylfentanyl, 4-methoxymethylfentanyl, 4-methylfentanyl, carfentanil, fentanyl, lofentanil, meperidine, remifentanil, and sufentanil.

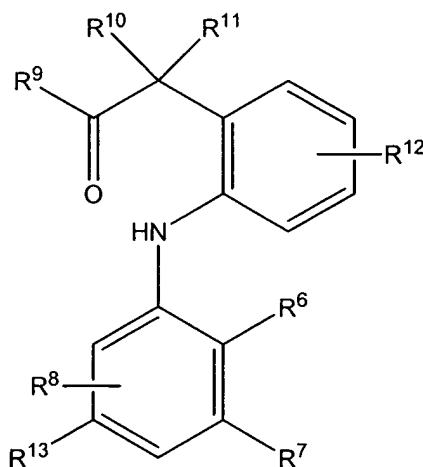
10. The salt of a codrug according to claim 2, wherein the active form of the opioid is an analgesic opioid.

25 11. The salt of a codrug according to claim 3, wherein the second drug moiety is an NSAID.

12. The salt of a codrug according to claim 11, wherein the NSAID is selected from piroxicam, diclofenac, etodolac, indomethacin, ketoralac, oxaprozin, tolmetin, naproxen, flubiprofen, fenoprofen, ketoprofen, ibuprofen, mefenamic acid, sulindac, apazone, phenylbutazone, aspirin, celecoxib and rofecoxib, and derivatives thereof.

5 13. The salt of a codrug according to claim 11, wherein the active form of the NSAID is diclofenac or a diclofenac derivative.

14. The salt of a codrug according to claim 11, wherein the active form of the NSAID is represented in the general formula (III):



(III)

wherein

R⁶ is a lower alkyl, a lower alkoxy, a fluoro, or a chloro;

R⁷ and R⁸ are each, independently for each occurrence, a hydrogen, a lower alkyl, a fluoro, a chloro, or a trifluoromethyl;

15 R⁹ is OH;

R¹⁰ is a hydrogen or a lower alkyl;

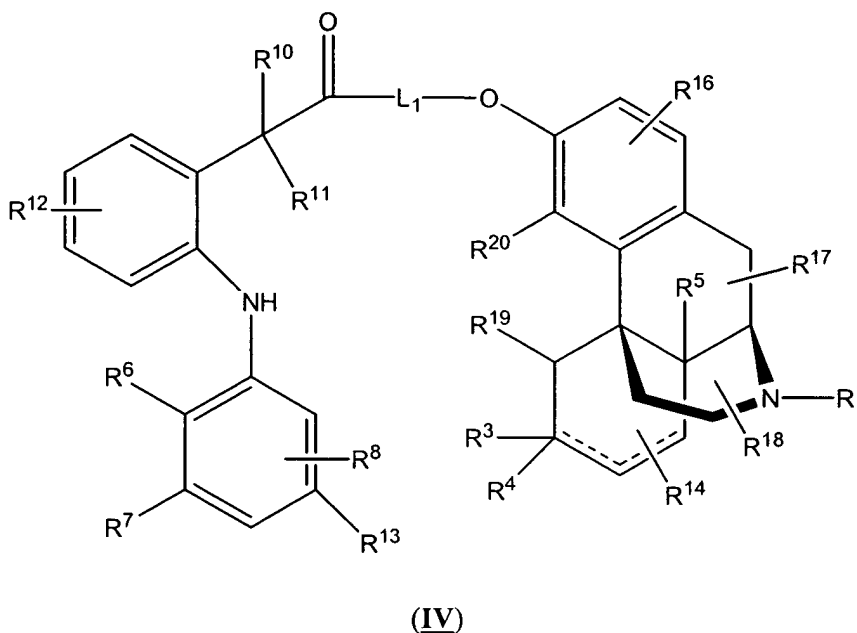
R¹¹ is a hydrogen, a lower alkyl, or when R¹⁰ is hydrogen, benzyl;

R¹² is a hydrogen, a lower alkyl, a lower alkoxy, a fluoro, a chloro, or a bromo;

R¹³ is hydrogen or trifluoromethyl when R⁶ is hydrogen or chloro and R⁷ is hydrogen or trifluoromethyl.

20

15. The salt of a codrug according to claim 1, wherein the codrug is represented by the general formula (IV):



5 wherein

L_1 is absent or represents a linkage;

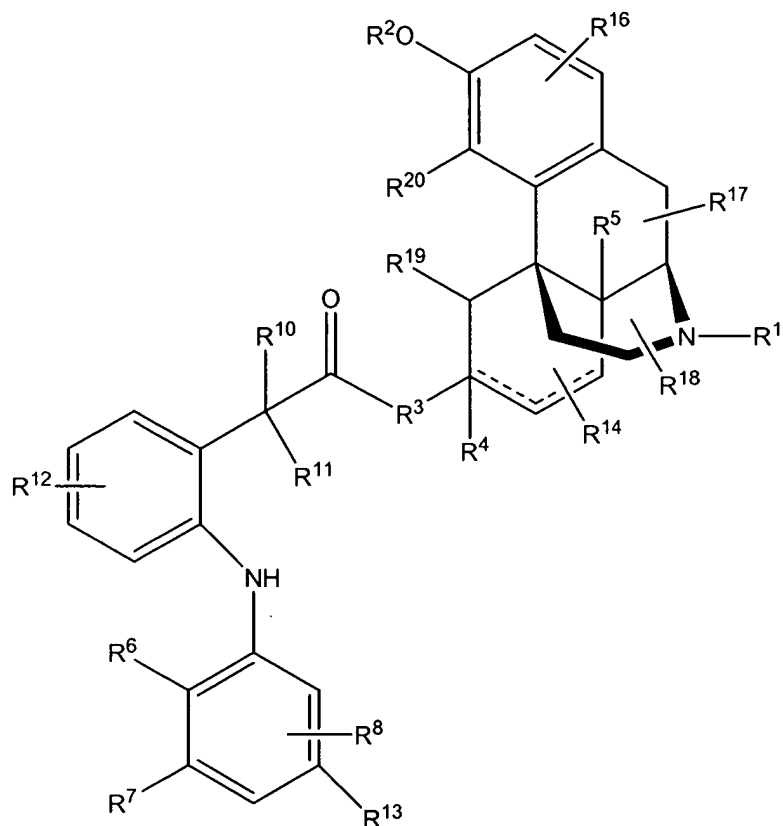
R^1 represents a hydrogen, a C_{1-6} -alkyl group, a C_{3-6} -cycloalkyl- C_{1-6} -alkyl group, a C_{1-6} -alkenyl group, a C_{1-6} -alkanoyl group, a C_{3-6} -cycloalkenyl- C_{1-6} -alkyl group, a C_{3-6} -cycloalkyl- C_{1-6} -alkanoyl group, a C_{3-6} -cycloalkenyl- C_{1-6} -alkanoyl group, an Ar- C_{1-6} -alkyl group, or an allyl group;

10 R^3 represents a hydrogen, a C_{1-6} -alkylthio group, an aryl group, a C_{1-6} -alkoxycarbonylalkyl group, a C_{1-6} -alkyl group, a hydroxyl group, an azido group, a C_{1-12} -alkanoyl group, an amine NR^d_2 wherein R^d is hydrogen or Ar, or $C(=O)NH_2$ when R^4 is a hydrogen, or an oxo group or $=NOH$ when R^4 is absent;

15 R^4 is absent or represents a hydrogen;

20 R^5 represents a hydrogen, a hydroxyl group, a lower alkyl group, an amine NR_aR_b wherein R_a is a hydrogen, alkyl C_{1-12} , alkenyl C_{3-8} , cycloalkyl C_{3-7} alkyl C_{1-4} , Ar-alkyl C_{1-5} or Ar-alkenyl C_{3-5} , provided that R_a does not contain the system $-CH=CH-$ attached to the nitrogen atom; and R_b is hydrogen, alkyl C_{1-8} , or

- the group COR_c wherein R_c is a hydrogen, alkyl C_{1-11} , alkenyl C_{2-7} , Ar, Ar-alkyl C_{1-5} , Ar-alkenyl C_{2-5} , cycloalkyl C_{3-8} , or cycloalkyl C_{3-8} alkyl C_{1-3} ;
- or R^4 and R^5 taken together represent $-(\text{CH}_2)_2-$;
- R^6 is a lower alkyl, a lower alkoxy, a fluoro, or a chloro;
- 5 R^7 and R^8 are each, independently for each occurrence, a hydrogen, a lower alkyl, a fluoro, a chloro, or a trifluoromethyl;
- R^{10} is a hydrogen or a lower alkyl;
- R^{11} is a hydrogen, a lower alkyl or when R^{10} is hydrogen, benzyl;
- R^{12} is a hydrogen, a lower alkyl, a lower alkoxy, a fluoro, a chloro, or a bromo;
- 10 R^{13} is hydrogen or trifluoromethyl when R^6 is hydrogen or chloro and R^7 is hydrogen or trifluoromethyl;
- R^{14} represents a hydrogen, a lower alkyl group, a halogen group, or $-\text{C}(-\text{OH})(-\text{R}^{15})_2$;
- R^{15} independently for each occurrence represents a lower alkyl;
- R^{16} , R^{17} , and R^{18} each independently represent a hydrogen, a lower alkyl group, or a
- 15 halogen group;
- R^{19} and R^{20} each represent hydrogen or together represent the oxygen of a dihydrofuran ring;
- Ar is phenyl or phenyl substituted by halogen, alkyl C_{1-3} , hydroxyl or alkoxy C_{1-3} ; and the dotted line indicates an optional bond.
- 20 16. The salt of a codrug according to claim 1, wherein the codrug is represented by the general formula (V):



(V)

wherein

- 5 R^1 represents a hydrogen, a C_{1-6} -alkyl group, a C_{3-6} -cycloalkyl- C_{1-6} -alkyl group, a C_{1-6} -alkenyl group, a C_{1-6} -alkanoyl group, a C_{3-6} -cycloalkenyl- C_{1-6} -alkyl group, a C_{3-6} -cycloalkyl- C_{1-6} -alkanoyl group, a C_{3-6} -cycloalkenyl- C_{1-6} -alkanoyl group, an Ar- C_{1-6} -alkyl group, or an allyl group;
- R^2 represents a hydrogen, a C_{1-6} -alkyl group, or a C_{1-6} -alkanoyl group;
- R^3 is absent or represents a linkage;
- 10 R^4 is absent or represents a hydrogen;
- R^5 represents a hydrogen, a hydroxyl group, a lower alkyl group, an amine NR_aR_b wherein R_a is a hydrogen, alkyl C_{1-12} , alkenyl C_{3-8} , cycloalkyl C_{3-7} alkyl C_{1-4} , Ar-alkyl C_{1-5} or Ar-alkenyl C_{3-5} , provided that R_a does not contain the system $-CH=CH-$ attached to the nitrogen atom; and R_b is hydrogen, alkyl C_{1-8} , or the group COR_c wherein R_c is a hydrogen, alkyl C_{1-11} , alkenyl C_{2-7} , Ar, Ar-alkyl C_{1-5} , Ar-alkenyl C_{2-5} , cycloalkyl C_{3-8} , or cycloalkyl C_{3-8} alkyl C_{1-3} ;
- 15

or R⁴ and R⁵ taken together represent $-(CH_2)_2-$;

R⁶ is a lower alkyl, a lower alkoxy, a fluoro, or a chloro;

R⁷ and R⁸ are each, independently for each occurrence, a hydrogen, a lower alkyl, a fluoro, a chloro, or a trifluoromethyl;

5 R¹⁰ is a hydrogen or a lower alkyl;

R¹¹ is a hydrogen, a lower alkyl or when R¹⁰ is hydrogen, benzyl;

R¹² is a hydrogen, a lower alkyl, a lower alkoxy, a fluoro, a chloro, or a bromo;

R¹³ is hydrogen or trifluoromethyl when R⁶ is hydrogen or chloro and R⁷ is hydrogen or trifluoromethyl;

10 R¹⁴ represents a hydrogen, a lower alkyl group, a halogen group, or $-C(-OH)(-R^{15})_2$;

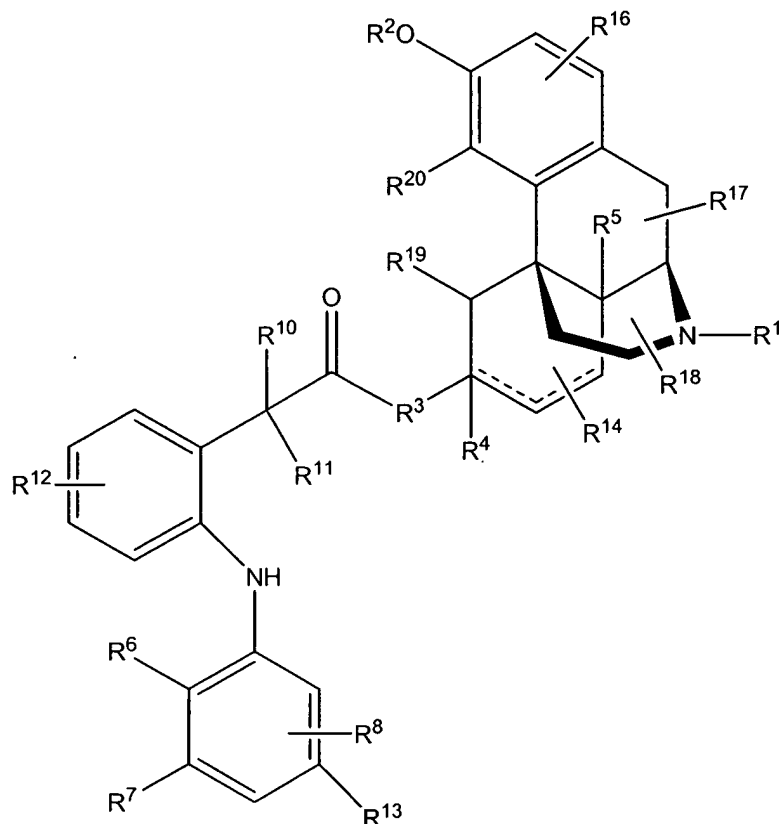
R¹⁵ independently for each occurrence represents a lower alkyl;

R¹⁶, R¹⁷, and R¹⁸ each independently represent a hydrogen, a lower alkyl group, or a halogen group;

15 R¹⁹ and R²⁰ each represent hydrogen or together represent the oxygen of a dihydrofuran ring;

Ar is phenyl or phenyl substituted by halogen, alkyl C₁₋₃, hydroxyl or alkoxy C₁₋₃; and the dotted line indicates an optional bond.

17. The salt of a codrug according to claim 1, wherein the codrug is represented by the general formula (V):



(V)

wherein

5 R^1 represents a hydrogen, a C_{1-6} -alkyl group, a C_{3-6} -cycloalkyl- C_{1-6} -alkyl group, a C_{1-6} -alkenyl group, a C_{1-6} -alkanoyl group, a C_{3-6} -cycloalkenyl- C_{1-6} -alkyl group, a C_{3-6} -cycloalkyl- C_{1-6} -alkanoyl group, a C_{3-6} -cycloalkenyl- C_{1-6} -alkanoyl group, an Ar- C_{1-6} -alkyl group, or an allyl group;

R^2 represents a hydrogen, a C_{1-6} -alkyl group, or a C_{1-6} -alkanoyl group;

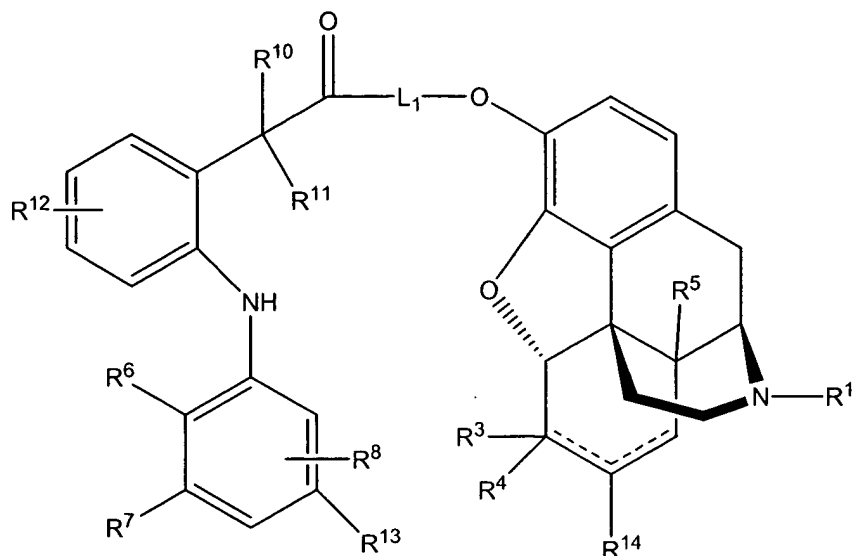
10 R^3 represents an oxygen, a C_{1-6} -alkylthio group, an aryl group, a C_{1-6} -alkoxycarbonylalkyl group, a C_{1-6} -alkyl group, an azido group, a C_{1-12} -alkanoyl group, an amine NR^d_2 (wherein R^d , independently for each occurrence, is hydrogen, a C_{1-6} -alkyl group, or Ar), $-C(=O)NH-$ when R^4 is a hydrogen, or $=NO-$ when R^4 is absent;

R^4 is absent or represents a hydrogen;

15 R^5 represents a hydrogen, a hydroxyl group, a lower alkyl group, an amine NR_aR_b wherein R_a is a hydrogen, alkyl C_{1-12} , alkenyl C_{3-8} , cycloalkyl C_{3-7} alkyl C_{1-4} ,

- Ar-alkyl C₁₋₅ or Ar-alkenyl C₃₋₅, provided that R_a does not contain the system –CH=CH– attached to the nitrogen atom; and R_b is hydrogen, alkyl C₁₋₈, or the group COR_c wherein R_c is a hydrogen, alkyl C₁₋₁₁, alkenyl C₂₋₇, Ar, Ar-alkyl C₁₋₅, Ar-alkenyl C₂₋₅, cycloalkyl C₃₋₈, or cycloalkyl C₃₋₈ alkyl C₁₋₃;
- 5 or R⁴ and R⁵ taken together represent –(CH₂)₂–;
- R⁶ is a lower alkyl, a lower alkoxy, a fluoro, or a chloro;
- R⁷ and R⁸ are each, independently for each occurrence, a hydrogen, a lower alkyl, a fluoro, a chloro, or a trifluoromethyl;
- R¹⁰ is a hydrogen or a lower alkyl;
- 10 R¹¹ is a hydrogen, a lower alkyl or when R¹⁰ is hydrogen, benzyl;
- R¹² is a hydrogen, a lower alkyl, a lower alkoxy, a fluoro, a chloro, or a bromo;
- R¹³ is hydrogen or trifluoromethyl when R⁶ is hydrogen or chloro and R⁷ is hydrogen or trifluoromethyl;
- R¹⁴ represents a hydrogen, a lower alkyl group, a halogen group, or –C(–OH)(–R¹⁵)₂;
- 15 R¹⁵ independently for each occurrence represents a lower alkyl;
- R¹⁶, R¹⁷, and R¹⁸ each independently represent a hydrogen, a lower alkyl group, or a halogen group;
- R¹⁹ and R²⁰ each represent hydrogen or together represent the oxygen of a dihydrofuran ring;
- 20 Ar is phenyl or phenyl substituted by halogen, alkyl C₁₋₃, hydroxyl or alkoxy C₁₋₃; and the dotted line indicates an optional bond.

18. The salt of a codrug according to claim 1, wherein the codrug is represented by the general formula **(VI)**:



(VI)

wherein

L₁ is absent or represents a linkage;

- 5 R¹ represents a hydrogen, a C₁₋₆-alkyl group, a C₃₋₆-cycloalkyl-C₁₋₆-alkyl group, a C₁₋₆-alkenyl group, a C₁₋₆-alkanoyl group, a C₃₋₆-cycloalkenyl-C₁₋₆-alkyl group, a C₃₋₆-cycloalkyl-C₁₋₆-alkanoyl group, a C₃₋₆-cycloalkenyl-C₁₋₆-alkanoyl group, an Ar-C₁₋₆-alkyl group, or an allyl group;

- 10 R³ represents a hydrogen, a C₁₋₆-alkylthio group, an aryl group, a C₁₋₆-alkoxycarbonylalkyl group, a C₁₋₆-alkyl group, a hydroxyl group, an azido group, a C₁₋₁₂-alkanoyl group, an amine NR^d₂ wherein R^d is hydrogen or Ar, or C(=O)NH₂ when R⁴ is a hydrogen, or an oxo group or =NOH when R⁴ is absent;

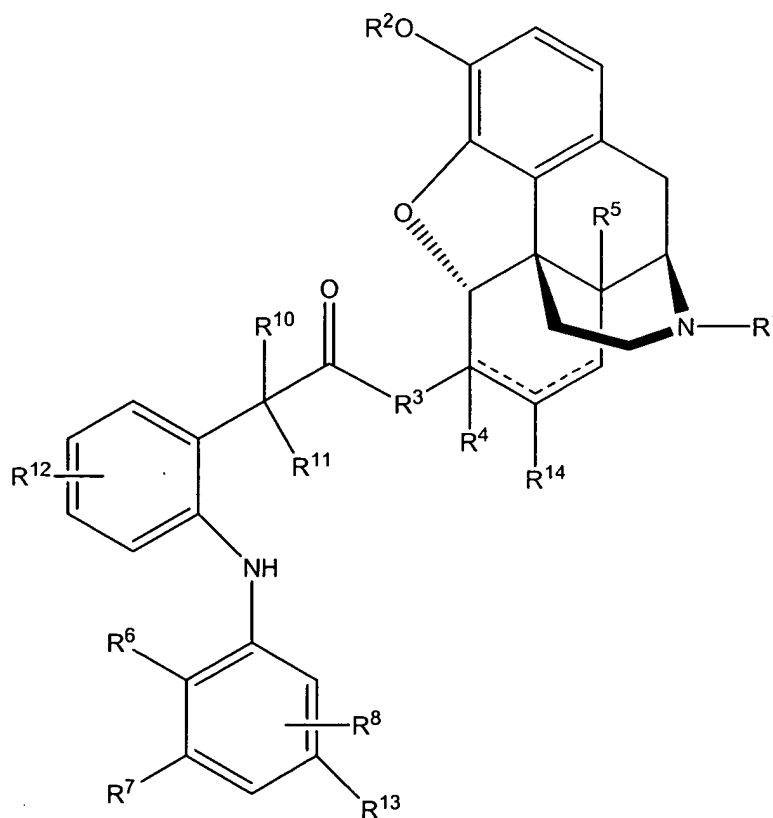
R⁴ is absent or represents a hydrogen;

- 15 R⁵ represents a hydrogen, a hydroxyl group, a lower alkyl group, an amine NR_aR_b wherein R_a is a hydrogen, alkyl C₁₋₁₂, alkenyl C₃₋₈, cycloalkyl C₃₋₇ alkyl C₁₋₄, Ar-alkyl C₁₋₅ or Ar-alkenyl C₃₋₅, provided that R_a does not contain the system -CH=CH- attached to the nitrogen atom; and R_b is hydrogen, alkyl C₁₋₈, or the group COR_c wherein R_c is a hydrogen, alkyl C₁₋₁₁, alkenyl C₂₋₇, Ar, Ar-alkyl C₁₋₅, Ar-alkenyl C₂₋₅, cycloalkyl C₃₋₈, or cycloalkyl C₃₋₈ alkyl C₁₋₃;

20 or R⁴ and R⁵ taken together represent -(CH₂)₂-;

- R^6 is a lower alkyl, a lower alkoxy, a fluoro, or a chloro;
 R^7 and R^8 are each, independently for each occurrence, a hydrogen, a lower alkyl, a fluoro, a chloro, or a trifluoromethyl;
 R^{10} is a hydrogen or a lower alkyl;
 5 R^{11} is a hydrogen, a lower alkyl or when R^{10} is hydrogen, benzyl;
 R^{12} is a hydrogen, a lower alkyl, a lower alkoxy, a fluoro, a chloro, or a bromo;
 R^{13} is hydrogen or trifluoromethyl when R^6 is hydrogen or chloro and R^7 is hydrogen or trifluoromethyl;
 R^{14} represents a hydrogen, a lower alkyl group, a halogen group, or $-C(-OH)(-R^{15})_2$;
 10 Ar is phenyl or phenyl substituted by halogen, alkyl C_{1-3} , hydroxyl or alkoxy C_{1-3} ;
 and the dotted line indicates an optional bond.

19. The salt of a codrug according to claim 1, wherein the codrug is represented by the general formula (VII):



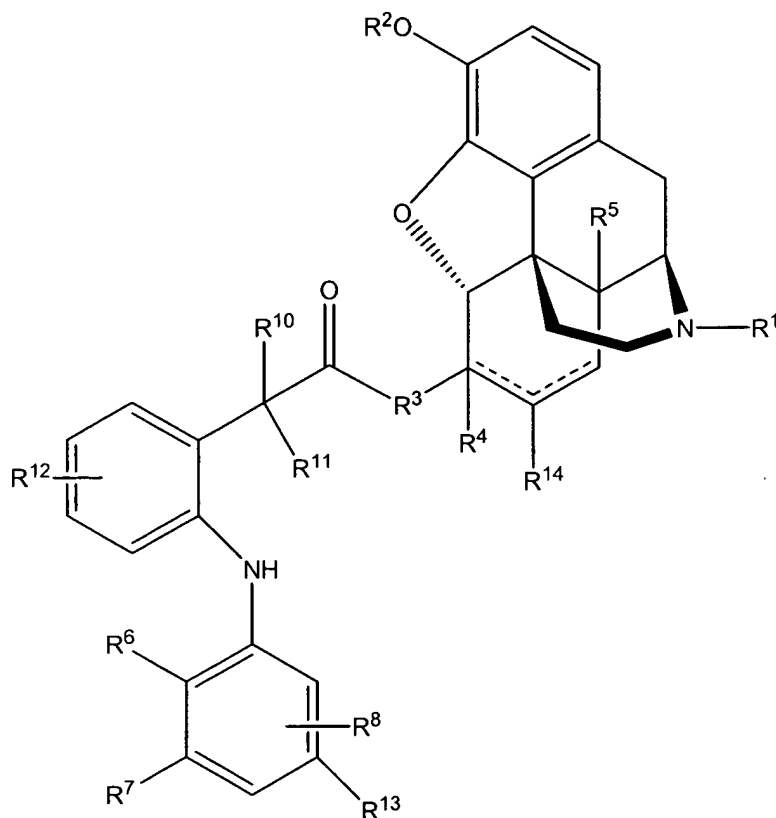
(VII)

15

wherein

- R^1 represents a hydrogen, a C_{1-6} -alkyl group, a C_{3-6} -cycloalkyl- C_{1-6} -alkyl group, a C_{1-6} -alkenyl group, a C_{1-6} -alkanoyl group, a C_{3-6} -cycloalkenyl- C_{1-6} -alkyl group, a C_{3-6} -cycloalkyl- C_{1-6} -alkanoyl group, a C_{3-6} -cycloalkenyl- C_{1-6} -alkanoyl group, an Ar- C_{1-6} -alkyl group, or an allyl group;
- R^2 represents a hydrogen, a C_{1-6} -alkyl group, or a C_{1-6} -alkanoyl group;
- R^3 is absent or represents a linkage;
- R^4 is absent or represents a hydrogen;
- R^5 represents a hydrogen, a hydroxyl group, a lower alkyl group, an amine NR_aR_b wherein R_a is a hydrogen, alkyl C_{1-12} , alkenyl C_{3-8} , cycloalkyl C_{3-7} alkyl C_{1-4} , Ar-alkyl C_{1-5} or Ar-alkenyl C_{3-5} , provided that R_a does not contain the system $-CH=CH-$ attached to the nitrogen atom; and R_b is hydrogen, alkyl C_{1-8} , or the group COR_c wherein R_c is a hydrogen, alkyl C_{1-11} , alkenyl C_{2-7} , Ar, Ar-alkyl C_{1-5} , Ar-alkenyl C_{2-5} , cycloalkyl C_{3-8} , or cycloalkyl C_{3-8} alkyl C_{1-3} ;
- or R^4 and R^5 taken together represent $-(CH_2)_2-$;
- R^6 is a lower alkyl, a lower alkoxy, a fluoro, or a chloro;
- R^7 and R^8 are each, independently for each occurrence, a hydrogen, a lower alkyl, a fluoro, a chloro, or a trifluoromethyl;
- R^{10} is a hydrogen or a lower alkyl;
- R^{11} is a hydrogen, a lower alkyl or when R^{10} is hydrogen, benzyl;
- R^{12} is a hydrogen, a lower alkyl, a lower alkoxy, a fluoro, a chloro, or a bromo;
- R^{13} is hydrogen or trifluoromethyl when R^6 is hydrogen or chloro and R^7 is hydrogen or trifluoromethyl;
- R^{14} represents a hydrogen, a lower alkyl group, a halogen group, or $-C(-OH)(-R^{15})_2$;
- Ar is phenyl or phenyl substituted by halogen, alkyl C_{1-3} , hydroxyl or alkoxy C_{1-3} ;
- and the dotted line indicates an optional bond.

20. The salt of a codrug according to claim 1, wherein the codrug is represented by the general formula (VII):



(VII)

wherein

- 5 R^1 represents a hydrogen, a C_{1-6} -alkyl group, a C_{3-6} -cycloalkyl- C_{1-6} -alkyl group, a C_{1-6} -alkenyl group, a C_{1-6} -alkanoyl group, a C_{3-6} -cycloalkenyl- C_{1-6} -alkyl group, a C_{3-6} -cycloalkyl- C_{1-6} -alkanoyl group, a C_{3-6} -cycloalkenyl- C_{1-6} -alkanoyl group, an Ar- C_{1-6} -alkyl group, or an allyl group;
- R^2 represents a hydrogen, a C_{1-6} -alkyl group, or a C_{1-6} -alkanoyl group;
- 10 R^3 represents a C_{1-6} -alkylthio group, an aryl group, a C_{1-6} -alkoxycarbonylalkyl group, a C_{1-6} -alkyl group, an oxygen, an azido group, a C_{1-12} -alkanoyl group, an amine NR^d_2 (wherein R^d , independently for each occurrence, is hydrogen, a C_{1-6} -alkyl group, or Ar), $-C(=O)NH-$ when R^4 is a hydrogen, or $=NO-$ when R^4 is absent;
- R^4 is absent or represents a hydrogen;
- 15 R^5 represents a hydrogen, a hydroxyl group, a lower alkyl group, an amine NR_aR_b wherein R_a is a hydrogen, alkyl C_{1-12} , alkenyl C_{3-8} , cycloalkyl C_{3-7} alkyl C_{1-4} ,

- Ar-alkyl C₁₋₅ or Ar-alkenyl C₃₋₅, provided that R_a does not contain the system –CH=CH– attached to the nitrogen atom; and R_b is hydrogen, alkyl C₁₋₈, or the group COR_c wherein R_c is a hydrogen, alkyl C₁₋₁₁, alkenyl C₂₋₇, Ar, Ar-alkyl C₁₋₅, Ar-alkenyl C₂₋₅, cycloalkyl C₃₋₈, or cycloalkyl C₃₋₈ alkyl C₁₋₃;
- 5 or R⁴ and R⁵ taken together represent –(CH₂)₂–;
- R⁶ is a lower alkyl, a lower alkoxy, a fluoro, or a chloro;
- R⁷ and R⁸ are each, independently for each occurrence, a hydrogen, a lower alkyl, a fluoro, a chloro, or a trifluoromethyl;
- R¹⁰ is a hydrogen or a lower alkyl;
- 10 R¹¹ is a hydrogen, a lower alkyl or when R¹⁰ is hydrogen, benzyl;
- R¹² is a hydrogen, a lower alkyl, a lower alkoxy, a fluoro, a chloro, or a bromo;
- R¹³ is hydrogen or trifluoromethyl when R⁶ is hydrogen or chloro and R⁷ is hydrogen or trifluoromethyl;
- R¹⁴ represents a hydrogen, a lower alkyl group, a halogen group, or –C(–OH)(–R¹⁵)₂;
- 15 Ar is phenyl or phenyl substituted by halogen, alkyl C₁₋₃, hydroxyl or alkoxy C₁₋₃; and the dotted line indicates an optional bond.
21. The salt of a codrug according to claim 17 or 20, wherein R³ represents a C₁₋₆-alkylthio group, an aryl group, a C₁₋₆-alkoxycarbonylalkyl group, a C₁₋₆-alkyl group, an oxygen, an azido group, a C₁₋₁₂-alkanoyl group, an amine NR^d₂ (wherein
- 20 R^d, independently for each occurrence, is hydrogen or Ar), –C(=O)NH– when R⁴ is a hydrogen, or =NO– when R⁴ is absent.
22. The salt of a codrug according to claim 2, wherein the first drug moiety is morphine and the second drug moiety is diclofenac.
23. The salt of a codrug according to claim 1, wherein the linkage is hydrolyzed
- 25 in bodily fluid.
24. The salt of a codrug according to claim 20, wherein the linkage includes one or more hydrolyzable groups selected from an ester, an amide, a carbamate, a carbonate, a cyclic ketal, a thioester, a thioamide, a thiocarbamate, a thiocarbonate, a xanthate and a phosphate ester.

25. The salt of a codrug according to claim 1, wherein the linkage is enzymatically cleaved.
26. The salt of a codrug according to claim 1, wherein the linkage includes a polyethylene glycol, a glycerol, a sugar, an alkylene chain, an amino acid, or an oligopeptide.
27. The salt of a codrug according to claim 1, wherein said codrug salt includes a counterion capable of protonating the basic amine.
28. The salt of a codrug according to claim 1, wherein said codrug salt is formulated from an organic acid.
29. The salt of a codrug according to claim 25, wherein said organic acid is selected from maleic acid, malonic acid, oxalic acid, tartaric acid, citric acid, lactic acid, fumaric acid, benzoic acid, p-toluenesulfonic acid, methanesulfonic acid, acetic acid, adipic acid, formic acid, and salicylic acid.
30. The salt of a codrug according to claim 1, wherein said codrug salt is formulated from an inorganic acid.
31. The salt of a codrug according to claim 27, wherein said inorganic acid is selected from hydrochloric acid, sulfuric acid, hydrobromic acid, nitric acid, and phosphoric acid.
32. The salt of a codrug according to claim 1, wherein the salt of the codrug has a decomposition rate at room temperature less than 10% of the decomposition rate of said codrug as a free base.
33. The salt of a codrug according to claim 1, wherein the salt of the codrug has a decomposition rate at room temperature less than 1% of the decomposition rate of said codrug as a free base.

34. The salt of a codrug according to claim 1, wherein the codrug has an ED₅₀ for each of said first and second biological activities at least 10 times greater than the ED₅₀ of said regenerated first and second drug moieties as active agents.
35. The salt of a codrug according to claim 1, wherein the codrug has an ED₅₀ for each of said first and second biological activities at least 1000 times greater than the ED₅₀ of said regenerated first and second drug moieties as active agents.
36. The salt of a codrug according to claim 1, which is essentially insoluble in body fluids.
37. The salt of a codrug according to claim 32, wherein said regenerated first and second drug moieties are at least 10 times more soluble than said codrug salt.
38. A malonic acid salt of a codrug comprising morphine covalently linked to diclofenac by a bond which is hydrolyzable to regenerate active morphine and diclofenac *in vivo*.
39. The salt of a codrug according to claim 1, wherein the salt includes the codrug and a pharmaceutically active counterion.
40. A method of manufacturing a salt of a codrug according to claim 1, comprising conjugating an opioid and an NSAID, and crystallizing the codrug salt.
41. A pharmaceutical composition of a codrug salt according to claim 1, wherein the codrug salt is combined with a pharmaceutically acceptable excipient.
42. The salt of a codrug according to claim 1, wherein the codrug salt is dispersed in a hydrogel.
43. The salt of a codrug according to claim 1, wherein the codrug salt has a purity greater than the purity of the codrug as a free base.

44. The salt of a codrug according to claim 40, wherein the codrug salt has a purity of at least 97%.
45. A pharmaceutically acceptable salt of a codrug according to claim 1, wherein at least three drugs are linked to one another covalently.
- 5 46. A pharmaceutically acceptable salt of a codrug according to claim 1, wherein release of the active drugs follows pseudo-zero-order kinetics.
47. A pharmaceutically acceptable salt of a codrug according to claim 1, wherein the drugs are covalently linked and release of the active drugs follows pseudo-zero-order kinetics for about 10 days to about 6 weeks.
- 10 48. A pharmaceutically acceptable salt of a codrug according to claim 44, wherein release of each active drug follows pseudo-zero-order kinetics for about 3 weeks.
49. A pharmaceutically acceptable salt of a codrug according to claim 1, which is soluble in body fluids.
- 15 50. A pharmaceutically acceptable salt of a codrug according to claim 1, wherein said salt form is formulated from an acid that treats at least one symptom of a condition.
51. A method of relieving pain comprising administering an effective amount of a pharmaceutically acceptable salt of a codrug according to claim 1 to a patient in
20 need of pain relief.
52. The salt of a codrug according to claim 1, wherein the first and second drug moieties are different.
53. The salt of a codrug according to claim 1, wherein the first and second drug moieties are the same.